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COAGULATING ACTIVITY OF THE BLOOD, VASCULAR WALL,  
AND MYOCARDIUM UNDER HYPODYNAMIA CONDITIONS

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The lack of information about the status of hemocoagulation, thrombocyte activity, and other coagulating factors of the blood and vascular wall during restricted movement has necessitated experimental observations on this problem [Tyavokin, 1966].\*\*

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The coagulating properties of the blood, vascular wall, and myocardium during hypodynamia in animals was studied.

Of 131 chinchilla rabbits weighing 2-3 kg, 75 were kept in hypodynamia for 3, 7, 14, 30, 45, and 60 days, and 56 control animals were kept under normal conditions for the same periods. Limitation of the animals' movement was accomplished through the use of special cages, as suggested by V.V. Tyavokin. Blood from the marginal vein of the rabbits' ears was collected in silicon-impregnated test tubes and stabilized with sodium citrate in a 1:9 ratio, after which the animals were sacrificed and 1:10 extracts were prepared from the aorta (by layers), myocardium, and venae cavae. Preparations from the myocardium, aortic arch, and abdominal aorta were stained with fuchsin resorcinol using Weigert's method, halcyon blue using Stidman's method, and toluidine blue with subsequent enzymatic control by hyaluronidase; the Schiff reaction and Cross's method were used to show calcium crystals.

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The general coagulating activity of the blood increased sharply by the 14th day of the experiment (by 41.6%), but later decreased, reaching a minimum by the 60th day of the experiment (by 18% relative to controls). Antiheparin activity increased until the 14th day (2.3 times) and markedly dropped until the 30th day of the study (1.4 times), and then again increased. During the course of the experiment the thromboplastic properties of the blood intensified 17.7%, on the 30-45th day of the experiment they became lower than

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\*Numbers in the margin indicate pagination in the foreign text.

\*\* Translator's note: References not available.

the controls, and by the 60th day reached the initial level. Prothrombin activity also increased until the 14th day of the experiment (by 13%), and then decreased, becoming normal towards the later period of observation. The anticoagulating properties of the blood fell most significantly on the 14th day of the experiments, then increased and on the 60th day had a tendency to normalize. Fibrinase activity increased 30% until the 7th day of movement restriction, fell on the 14th day of the experiment, and then increased once again. A sharp increase of fibrinogen in the blood of the experimental animals on the 3rd day of hypodynamia (65.8% relative to controls) was replaced beginning with the 7th day of the experiment by a progressive decrease. Fibrinogen B sharply increased (13 times) until the 30th day of hypodynamia, then its quantity decreased, but remained higher than control. Fibrin and fibrin-monomer degradation products were discovered only in the plasma of animals kept in a motion-restricted regime for 7, 14, and 30 days. Fibrinolysis was depressed by the 14th day of the studies (by 34%), then increased maximally by the 45th day of movement restriction (by 19%) and approached control values on the 60th day of the experiment (Fig. 12).

The coagulating activity of thrombocytes, determined by the difference between results in thrombocyte and non-thrombocyte plasmas, also changed, depending upon the duration of the animals' stays in hypodynamic conditions. The overall coagulating capability of thrombocytes decreased most significantly on the 14th day of motion restriction, but later normalized. The antiheparin activity of platelets underwent similar dynamics. The thromboplastic potential of thrombocytes usually decreased until the 14th day of hypodynamia, but then exceeded the initial level. Prothrombin complex enzyme activity in the thrombocytes of the rabbits fell sharply on the third day of the experiment and reestablished itself on the 14th day of the experiment. Later, a second drop in blood platelet prothrombin activity was noted until the 45th day of motion restriction. The anticoagulating activity of platelets decreased somewhat on the third day of hypodynamia because of a decrease of free heparin in them. On the 7-14th day of the experiment, the anticoagulating /47 properties of thrombocytes and the level of heparin in them increased.

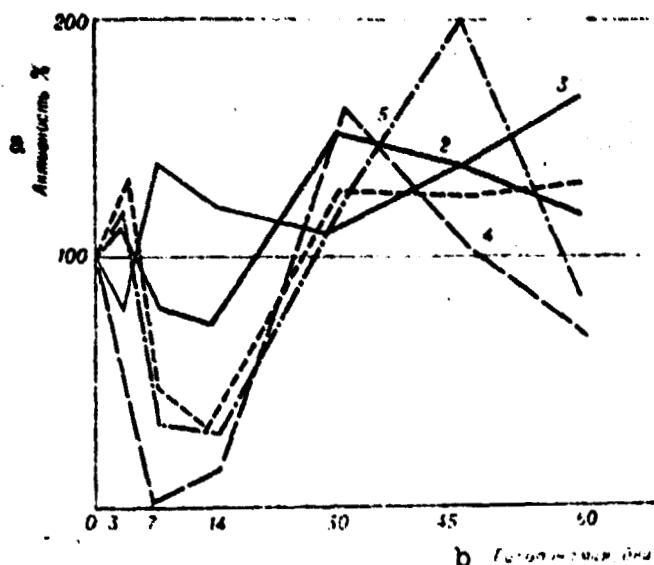


Fig. 12. The dynamics of overall coagulation, thromboplastic, and antiheparin activity of the blood during hypodynamia.

1 - whole blood coagulating time, Lee and White method; 2 - recalcification time; 3 - prothrombin consumption; 4 - anti-heparin activity; 5 - plasma tolerance to heparin; a - activity, %; b - hypodynamia, days.

adhesive activity, however the peak of these indices occurred on the 14th day of hypodynamia. Thrombocyte aggregation increased on the 3rd day due to an increase of all forms of aggregates. On the 7th day of the experiment, the overall quantity of conglomerates decreased, but the specific weight of middle- and large-size aggregates among them increased. There was a simultaneous change in the sensitivity of thrombocytes to various aggregating agents. By the 30th day of hypodynamia, the aggregating activity decreased due to a decrease in average and large-size conglomerates. Later, as a result of the decomposition of average and large-size aggregates, their general number increased (Fig. 13).

Restriction of movements was also accompanied by shifts in the tissue hemostatic system. The thromboplastic activity of the intima media of the aorta and myocardium did not change, and manifested itself until the extracts were diluted 10,000 times. The

Fibrinase activity increased somewhat on the third day of hypodynamia, fell sharply on the 7-14th day of the experiment, but increased again on the 45th day.

Thrombocyte quantity in the blood of experimental animals increased until the 7th day of the experiment (1.8 times), then gradually decreased, but did not reach the initial level. Similar changes occurred with the capability of blood platelets to stratify and with their

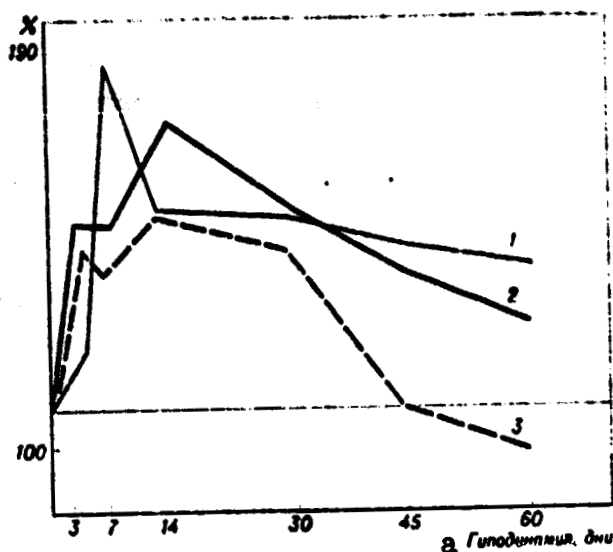


Fig. 13. The dynamics of the quantity of thrombocytes and their functional activity during hypodynamia.

1 - quantity of thrombocytes; 2 - adhesive index of thrombocytes; 3 - quantity of stratified thrombocytes; a - hypodynamia, days.

the aorta and myocardium decreased by the 7-14th day of observation, and on the 30-60th days reached the initial indices. Following a considerable (50%) decrease on the 14th day of the experiment, concentrations of antiheparin compounds in the veins were reestablished following a month of the animals' confinement in hypodynamic conditions.

Prothrombin complex enzyme activity in the tissues under study, except the intima, increased on the 3rd day of motion restriction, and on the 7th day differed from the indices of the control group of rabbits. Following an increase on the 3rd day of hypodynamia, the coagulating activity of the veins and myocardium steadily dropped until the 14th day, increased again following a month of the experiment, and again decreased by the 60th day of observation. Following the 7th day of immobilization, this index increased under the influence of the extracts from the middle and external layers of the aorta, then later did not differ from the controls.

The anticoagulating properties of the vessels and myocardium increased on the 3rd day of hypodynamia, then decreased on the 7th

thrombokinese properties of the external layer of the aorta decreased on the 7th day of the experiment, reached initial levels by the 14th day, and increased in later periods. Venous thromboplastin activity decreased 5 times by the 7-14th day of motion restriction, was reestablished on the 30th day, and again decreased by the 60th day of the experiment. The anti-heparin properties of

day. Later the anticoagulating activity of the vessels and myocardium increased right up to the 60th day of observation, but that of the intima returned to initial figures following the 30th day. The anticoagulating resources of the vessels and the myocardium increased due to both heparin and heparin-like compounds.

The fibrin-stabilizing activity of the aorta, myocardium, and venae cavae increased, reached a maximum by the 14th day of immobilization, and gradually decreased to control values by the end of the experiment. The vessels and myocardium of intact rabbits had a very low fibrinolytic activity. In the aorta, plasminogen activators appeared in insignificant quantities only in the adventitia. The concentration of fibrinolysis stimulators was higher in the veins than in the aorta. The low fibrinolytic activity of the vessels and myocardium was conditioned by the presence of powerful plasminogen inhibitors, the concentrations of which were higher in the internal and middle layers of the aorta. The content of fibrinolysis activators increased on the 3rd day of the experiment, dropped sharply by the 7th day, increased again following two weeks of the animals' stay in hypodynamia, then later remained the same. Despite the increase in the concentration of enzyme process catalysts on the third day, the fibrinolytic activity of the aorta, myocardium, and venae cavae was low due to their high content of fibrinolysis inhibitors. Only in the veins did the level of plasminogen inhibitors decrease following short term motionlessness. The fibrinolytic potential of the aorta, myocardium, and venae cavae decreased on the 7th day of hypodynamia, and increased somewhat following two weeks of immobilization. Following 30-60 days of observation, the quantity of fibrinolysis activators in the vascular wall and myocardium remained in the level of the 14th day, but their fibrinolytic potential increased significantly. Obviously, the speed of the enzymatic process is basically caused not by activators, but depressors of fibrinolysis, the concentrations of which dropped sharply in the later periods of the experiment.

During histologic study of preparations from the aorta, edema of the endothelium, subendothelium, and basal matter of the vascular

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wall appeared on the 3rd day of hypodynamia. Endothelial cells were enlarged and protruded into the vascular lumen. The number of connective tissue elements in the edematous basal matter of the vascular wall increased. In the altered endothelium, subendothelium, and interstitial matter of the middle layer of the aorta, a metachromatic substance appeared following 3 days of hypodynamia, a substance which disappeared after prior treatment of the aortic sections with hyaluronidase, which indicates the presence of acid mucopolysaccharides of the chondroitin sulfuric acid and chondroitin sulfate A and S types. After one or two weeks of the animals' stay under hypodynamic conditions the edema in the vascular wall intensified. Metachromatic staining increased from the adventitia to the intima. The greatest concentration of acid mucopolysaccharides was noted in the intima. Restriction of movement caused disruptions in the microcirculatory bed of the aortic adventitia. On the 14th day of hypodynamia, stasis, parietal and obstructive thrombi, dilatated venules, and stenosis of the arterioles was noted in the vessels of the adventitia. The changes in the elastic framework following two weeks of hypodynamia were of a pronounced nature. The elastic fibers were thickened and fragmented, and their intimic connection with the basal matter of the aorta was disrupted. Calcium crystal impregnation appeared along the paths of the altered elastic structures. At later periods of hypodynamia, plaques appeared in the aortic arch and aneurisma in the abdominal aorta. Vascular wall edema decreased in these periods of observation, but the development of connective tissue was intensified. Detritus and fragments of elastic fibers were concentrated at the center of the plaques, a pronounced reaction of fibroblasts and fibrocytes was noted at the periphery, as was the appearance of collagen fibers forming a fibrous capsule. The quantity of acid mucopolysaccharides in the center of the plaques decreased, but their concentration remained rather high at the periphery.

Hence, during the early periods of movement restriction edema of the endothelium, subendothelium, and basal matter developed in the aorta, as did an intensification of acid mucopolysaccharide synthesis. By the 7-14th days the elastic structures of the aorta were also involved in the process, which was shown by their swelling



and fragmentation, and the deposition of calcium crystals along the course of the membranes. Prolonged stays of the animals in hypodynamic conditions were conducive to the development of plaques and aneurysma (Fig. 14).



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Fig. 14. Changes in the wall of the aorta. 30× magnification.

- a - swelling of the intermediate matter and cellular elements (rabbit 9, hypodynamia for 3 days);
- b - calcium deposition in an atherosclerotic plaque (Koss + halcyon blue; rabbit 10, hypodynamia for 7 days).

In the early periods of motion restriction, hypercoagulemia developed in the rabbits' blood, particularly on the 14th day. The decrease in fibrinogen level, fibrinase activity, the number of blood platelets, and their coagulating properties, together with the increase in blood thromboplastic activity and the appearance of reliable symptoms of thrombinemia evidenced the development of intravascular coagulation in the experimental animals by the 14th day of the experiment. A more prolonged stay in hypodynamic conditions caused hypocoagulemia in the rabbits, which by the end of the second month of the experiment was replaced by normalization of the majority of the indices. Hemostatic changes during hypodynamia occurred as in the thrombohemorrhagic syndrome with a hypercoagulemic phase, which developed as a consequence of the appearance of active thromboplastic substances from the vascular walls in the bloodstream, and a phase of hypocoagulemia, which was the result of the consumption of hemocoagulation factors. Changes in the tissue hemostatic system were of a contrary nature. In the early periods of motion restriction, anticoagulating and fibrinolytic activity in the vascular wall and myocardium increased, with a simultaneous decrease in fibrin-stabilizing, and in the venae cavae thromboplastic, properties. The irregular accumulation of substances with pronounced anticoagulating activity in the vascular wall possibly led to local hemorrhaging in the vasa vasorum. Profibrinolysin was precipitated in the forming fibrin, which intensified the fibrinolytic properties of the vessels. The altered vascular wall was the source of active thrombogenic substances which entered into the bloodstream and resulted in disrupted hemocoagulation. The increase in thrombocyte functional activity which arose here was accompanied by blood circulation disturbances in various organs and tissues, among them the aorta and myocardium, which intensified even more the changes which were observed in them.

Change in the coagulating activity of the blood and tissues during hypodynamia manifests itself in the form of two interconnected and mutually conditioned syndromes: thrombohemorrhagic in the blood and hemorrhago-thrombotic in the tissues.